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Minireview

Transitioning Toward Evidence-Based Research in the Health Sciences for the XXI Century

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This article discusses some of the misconceptions of evidence-based research in the health sciences. It proposes that since not all treatments in medicine and dentistry can be evidence-based, clinical applications of the evidence-based process should become a specialty. The case is particularly evident in dentistry. Therefore dentistry is taken in this article as a model for discussion. We propose that to approach dentistry from the viewpoint of the patient-oriented evidence that matters (POEM) is perfectly acceptable so far as we also engage in the process of research evaluation and appraisal in dentistry (READ). We distinguish between dentistry based on the evidence, and evidence-based dentistry. We argue that when invoking an evidence-based approach to dentistry or medicine, it is not sufficient to establish the 'levels of evidence', but rather that all evidence-based clinical intervention must undergo the stringent process of evidence-based research so that clinical practice guidelines be revised based on the best available evidence.

Keywords: evidence-based research – levels of evidence – clinical practice guidelines

Misrepresentations in Evidence-Based Research in the Health Sciences

Evidence-based research in the health sciences is controversial for a variety of reasons that range from the perception that providing services to patients in medicine, dentistry, nursing and other health sciences has been based on research evidence for decades. Hence, there is nothing new. Alternatively, it has been voiced that if a given procedure has been performed to some degree of success for years, why bother to change, even if the best available evidence mandates that it should be discarded or updated (1). This polarity is particularly evident in dentistry because of the process by which certain dental protocols have evolved into common use today. Therefore, we take dentistry as a model for the discussion below, although it self-evident that

the points raised pertain to the applications and implications of evidence-research in medicine, nursing and other health sciences, as we progress into the XXI Century.

If evidence-based research in dentistry and in any other health sciences is to be simply a tool, a technique, a procedural approach complementary to our profession, then it is possible and even probable that conceptual and practical hurdles will soon emerge that will impair, rather than optimize patient treatment. It is likely that inappropriate evaluation of the evidence and misinterpretation of the research findings will be detrimental to clinical decision-making, and will engender ill-recommended modes of intervention. Continued misrepresentation of the field of evidence-based dentistry, its purpose and intent, and process and outcome, will do nothing more than to propagate the misconception that '*evidence-based dentistry does not work*'.

For example, if oral surgery, or restorative dentistry, or endodontics or any other specialized domain in our field was not considered a specialty *per se*, but were merely

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viewed as a set of technical skills, then undoubtedly the efficacy and effectiveness of our clinical interventions with patients with particular needs would be hindered. It is also the case that what characterizes a specialty in our profession is the fact that its domains are specific and circumscribed, and do not, for the most part overlap with those pertaining to other specialties. Case in point, diagnostic decision trees, modes of interventions, clinical practice guidelines, etc. that pertain to, say, the specialty of periodontics are distinct, for the most part from those used in, say, cosmetic dentistry. Certain decision-making criteria and intervention protocols are shared, and can be similar across specialties, but complete overlaps are relatively rare. What makes a specialty as such is distinctly its unique place in the field of dentistry: its niche in the profession with respect to its purpose, procedure and utility to the treatment of a specific group of patients.

Toward Evidence-Based Dentistry as a Specialty

The day is fast approaching when evidence-based dentistry will be recognized, as it should, as a specialty of the profession in its own right. Not all clinical problems can be reliably diagnosed and treated by general dentists or geriatric dentists or pedodontists: hence the need for specialists. In the same vein, not all domains of clinical dentistry can be handled in an evidence-based paradigm. That is to say, evidence-based dentistry is a specific approach to dentistry that is both selective and specialized, as for any other dental specialty.

To perform hospital dentistry ‘wearing the hat’ of the orthodontist might very well lead most to state, in error, that hospital dentistry ‘*does not work*’: in fact, it does work when performed correctly, by a trained professional, and in the appropriate context. In the same line of thought, to perform a root canal with a screwdriver and a hammer also does not work; but, when a trained specialist performs the correct protocol with the appropriate tools and materials, root canals do work. Likewise, to perform evidence-based dentistry incorrectly does not work—it cannot work, it will not work: as baking a chicken in a steamer will never work!

Toward the Frontiers of Knowledge in the Health Sciences: A Role for Evidence-Based Research

As we transition into dentistry in the XXI Century, we must realize, as professionals and as scientists, that the breadth and the depth of the fields that constitute our profession are evolving. Take the example of our increasing knowledge and understanding of the malleable nature of chromatin, the packaging structure of the genome. In every cell, including those of the oral mucosa,

keratinocytes, periodontal ligament fibroblasts, immune cells migrating into salivary gland or pulpal compartments and the like, normal physiological modulation, pathological responses and healing processes are modulated and regulated at the genomic and interactomic levels by processes of chromatin assembly, repair and rearrangement. DNA packaged in eu- or heterochromatin can be either coding (about 5% of the DNA known sequences at present), or non-coding. The function of the latter is yet unclear, and continues to be the subject of intense investigation. One early theory about these long stretches of DNA that do not belong to the coding genomic, proteonomic and interactomic reading frame, was that they might represent useless genetic material: hence the early nomenclature of ‘junk DNA’. Progress in our understanding of fundamental epigenetic processes have now led to the appreciation that far from being ‘junk’, these stretches of noncoding DNA most likely play a critical role in determining what, how and when certain genes are read, transcribed into RNA and translated into protein. In other words, non-coding DNA is most likely critical in regulating the reading frame of chromatin in every cell, including the in oral cavity. Any change or alteration in DNA, such as the insertion of viral DNA (e.g. papilloma virus, herpes virus, HIV-1) can be expected to alter the coding-to-non-coding DNA relationship in certain cells (2–4). With respect to dentistry, one easily realizes how such processes may interest cells within the oral cavity, or cell populations that immunosurveil the oral cavity [e.g. regulatory T-cells, CD4 + CD25 + FoxP3+, which appear to be favored targets for infection by HIV-1(3)].

That is to say, it is a plausible hypothesis that changes in non-coding DNA and chromatin packaging will be shown, within this decade or the next, to have a significant impact in our fundamental understanding of physiological and pathological processes in oral biology and medicine, and in the development and testing of new and improved treatment interventions in clinical dentistry.

In brief, current cutting-edge developments in epigenetic are at the frontier of dental diagnosis and treatment, and of our ability to integrate these new findings into clinical decision-making. Concerted efforts at critically evaluating epigenetic evidence by means of the evidence-based process will, no doubt, favor the transition of our profession into the modern and contemporary dentistry of the XXI Century.

The Evidence-Based Approach is not Panacea

That said, let us return to the discussion of the nature and the role of evidence-based dentistry at present. It is unquestionable that certain interventions in dentistry need not, or cannot be subjected to the evidence-based paradigm. Take, for example, water fluoridation: one could question whether it might be worthwhile or

necessary, with our current cumulative knowledge of public health dentistry, to review critically the research evidence that supports, or not, this particular preventive dentistry intervention. In this particular case, evidence-based dentistry is most probably not needed.

In a sense, this situation is akin to that of a superficial cavity in the enamel compartment of a molar: here an aggressive restoration involving a root canal, a crown or an implant is most likely uncalled for. By contrast, a carie that projects proximal to the pulp chamber, will, in all likelihood require aggressive restoration.

One Facet of Evidence-Based Dentistry: Levels of Evidence

Assessing 'What' was Done is not Sufficient

We must therefore define the contextual, the procedural, and the clinical domain of the field of evidence-based research in dentistry, as we have previously in the domain of medicine (5,6) Only then will we be able to validate the construct of this emerging specialty domain.

To begin to illustrate certain of the *sine qua* non-characteristics of effective evidence-based dentistry, let us return to the previous restorative dentistry example. Let us propose that, for the purpose of the sake of argument only, that, given of course certain restrictions pertaining to clinical assessment of the damaged tooth, health of the patient and osteology pertinent to the case, at the present level of our clinical expertise, an implant might be considered as the preferred restorative approach. Let us also, again the purpose of this discussion, propose the following nomenclature:

- (i) extraction & implant—'restoration level I',
- (ii) crown—'restoration level II',
- (iii) root canal—'restoration level III'.

Now, of course, we realize that there are other factors, in addition to, and clearly more clinically important than 'restoration level' that ought to be evaluated: such as functionality, survival, patient needs/wants, quality of life and satisfaction, cost and insurance coverage, etc. That is to say, as clinicians, it is self-evident that, in order to evaluate a given intervention within a specialty, it is not sufficient to determine 'what' was done (here, the type of restoration, expressed and semi-quantified as 'restoration level'). We must evaluate 'why', 'how' and 'with what outcome' the clinical procedure was done. Short of that, clinical evaluations will at best be superficial, imprecise and incorrect, and at worst they will be dangerously misleading for the well-being of the patients.

A seemingly perfect parallel can be obtained for any specialty of clinical dentistry. The danger to the patients we serve that emerge from inadequate, imprecise and superficial semi-quantification of 'what was done',

with no concern for 'why it was done', 'how it was done' and 'how the outcomes pertain to the patients', are gargantuan.

Levels of Evidence in Evidence-Based Research

It is also the case for the emerging specialty of evidence-based dentistry. We can evaluate a body of evidence based on 'what' was done, and in this manner rank and obtain a semi-quantification of the 'level of the evidence'. We might say, for instance, that systematic reviews and meta-analyses must obtain a 'level of evidence I', and that randomized controlled trials ought to rated 'level of evidence II'. Observational studies might thus be ranked lower, regardless of the fact that in certain domains of clinical dentistry it is often impossible to design a traditional randomized and well-controlled trial. Consequently, for certain domains of dentistry, where these supposed 'optimal' studies cannot be performed, the 'level of the evidence' is bound to be lower than (some vaguely accepted) standard.

In any specialty of dentistry—and in fact in medicine and any of the health sciences—, should we stop at a mere 'what was done' evaluation, such as exemplified above as the rather artificial 'restoration level', and with a purported semi-quantification of the type 'treatment level I or II or III', we would collectively be horrified. The concerted complaint over such lack of stringency of the clinical evaluation tools would undoubtedly muster generalized efforts toward improving clinical effectiveness and efficacy.

The Other Facet of Evidence-Based Dentistry

Cursory Evaluation of the Literature Based on the Levels of Evidence

The danger to the field of clinical medicine in general, and dentistry in particular, specifically for certain patients groups, which conclusions based on the 'level of evidence' could bring, is clearly enormous. Case in point, a recent communication (7) reported the evaluation of the 'level of evidence' for antibiotic prophylaxis. The mere fact that the studies reviewed were not the 'optimal' clinical trials (8), led the authors to conclude that the evidence for prophylaxis was insufficiently strong. This statement was as scientifically ill-founded (i.e. not based on sound criteria of evidence-based research in dentistry or medicine), as it was in wanton disregard to the safety of the patients, in light of what we know of the detrimental effects of the oral bacterial flora to the cardiovascular system in general and aortic and pulmonary valves in particular.

Procedurally, evidence-based dentistry, as any other specialty of our profession, goes beyond the evaluation of

‘what’ was done. It is not sufficient to establish in one quick overlook whether the evidence was obtained by means of a clinical trial or an observational study. It is insufficient, imprecise and dangerously simplistic to report a purported evaluation of the research evidence based merely on the ‘level of evidence’ (1,9,10).

The Process of Evidence-Based Research

Rather, and as all the dental specialties also defend, in order to evaluate correctly what was done, one must examine ‘how’ it was done, ‘why’ it was done, and ‘what might be the clinical outcomes’ (utility, patient satisfaction, etc.). That is why evidence-based dentistry consists of a process by which we evaluate the validity and the reliability of the evidence presented in each published report. We examine by means of stringent criteria issues of research methodology, research design and data analysis (1,9,10). We quantify this evaluation protocol, such that the literature that is examined by means of this stringent critical appraisal can be subjected to a process of disqualification of the evidence that is not acceptable (1,11–13). Only the evidence that survives acceptable analysis, based on the rigorous criteria mentioned earlier, is evaluated for an overarching analysis of the data across the published reports. Of course, in order for outcomes across several papers to be pulled into one overarching analysis (i.e. meta-analysis), they must be homogenous (Fig. 1).

That is to say, the process of the systematic evaluation of the evidence examines ‘how’ the research was done, as well as ‘why’. It establishes by means of scientific criteria which piece of evidence might be acceptable, and which not. It further obtains a statement of the over-arching outcomes, and discusses the consensus clinical implications in an effort to answer ‘what might be the clinical outcomes’ (1,14–16). The *Journal of Evidence Dental Practice* provides a good example of this process since it presents analysis and evaluation of research evidence both in terms of the ‘level of evidence’, and in the form of a detailed commentary and analysis of the research process and findings. This journal, *eCAM*, provides complete systematic reviews, as well as instructional papers that guide readers and prospective evidence-based researchers in the field.

In brief, to present arguments for or against a clinical intervention under the pretense and the disguise of evidence-based medicine or dentistry merely by showing ‘level of evidence’, but without providing a complete and systematic evaluation of the literature is ill-advised. It may be considered by some to be unethical because it misrepresents the state of clinical research and presents obvious risks for patient welfare. Others may even purport it to be blatant research misconduct because this simplistic approach to overview the evidence is a

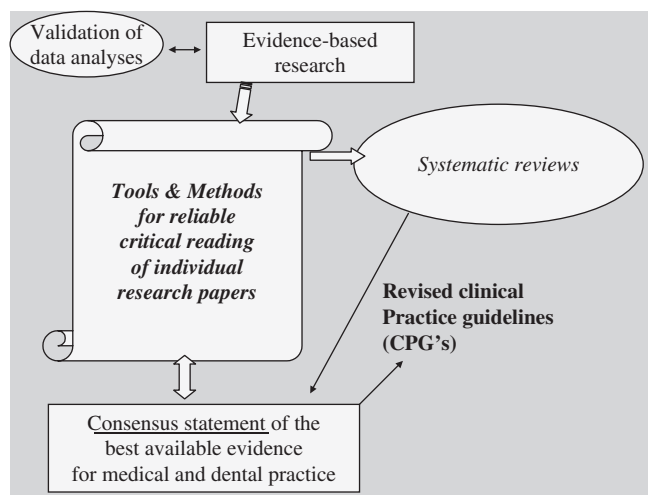


Figure 1. The process of evidence-based research, which corresponds from the validation of the data in published reports. The process involves the systematic and critical evaluation of the research reliability and validity of each published report pertaining to the PICO question. This is achieved by means of specialized evaluation instruments, which yield quantitative estimates of the strengths and the weakness of each report with respect to research design, methodology and statistical analysis. These estimates are assessed by means of acceptable sampling analysis, and when appropriate, by meta-analysis. The outcome of the systematic review process is the generation of the consensus statement, which leads to revisions of the clinical practice guidelines based on the best available research evidence [Note: an early version of this figure was published in (10); we present this modification here because it best represents the READ process].

wanton misrepresentation of the field, of the state of research and of the scientific process.

The Specialty of Evidence-Based Research: The Need to READ POEMs

Contextually, evidence-based research in dentistry pertains to two principal sub-fields that feed into each other, and necessitate each other. On the one hand, we have evidence-based research in dentistry, which focuses on the procedural approach to obtain the consensus statement of the best available evidence in the most valid and reliable manner. Sub-areas in evidence-based research involve, for example, the characterization of the instruments better adapted to evaluate the evidence (1,6, 9,11,13). Other topics include assessing the homogeneity versus bias of the evidence for meta-analysis (1,11,14). Evidence-based research, as an applied field, then is executed in the pursuit of identifying the best available treatment for a given intervention in clinical dentistry.

Implications for Patient Treatment

The second principal domain of evidence-based dentistry pertains to the implications and applications to

patient treatment. One important area of evidence-based dental practice addresses the translation of the consensus statement obtained through the research process just outlined into revised and updated clinical practice guidelines, and clinical decision-making. On the other hand, the day-to-day practice of dentistry may well increasingly evolve in years to come, such that dentists will increasingly base their clinical intervention on the best available research evidence, rather than on single pieces of immediately accessible evidence (17–19).

This dichotomy was cogently discussed in a recent editorial (20) by Michael Glick, chief editor of the *Journal of the American Dental Association*. The editorial discussed the relevance of the evidence-based process in the specific context of dentistry.

Toward READ

In brief, Glick defends the need and the utilization of research findings in the process of clinical decision-making. He argues with eloquence much in the vein of the points outlined above, that *‘...as much as possible...evidence-based dental practice guidelines should be based on the interpretation of research findings and their subsequent transfer into the clinical setting...(because) this greatly limits the influence of one particular person’s clinical experience on clinical practice guidelines...’* (20).

That is to say, Glick supports the view presented here that the emerging specialty of evidence-based dentistry will be practiced in the XXI Century with increasing and unwavering prudent reliance on research findings, following a critical and systematic process of research evaluation and appraisal in dentistry, which we could state as the acronym: READ (Fig. 1).

Glick further notes, however, certain limitations to practice of evidence-based dentistry. He emphasizes for instance that *‘...for the clinical expert to have a place in the hierarchy of EBD, the clinical expert’s knowledge and experience must be based on some kind of evidence...(and therefore) the clinical expert can provide the bridge between the science and the art of dentistry, and help fill the gap when evidence is weak or lacking...’* (20). Therefore, he correctly brings to the forefront the fact that the overall body of published research evidence in any given aspect of physiology and pathology—including the example of epigenetics outlined above—is fast rising. The ability of sifting through this body of information to determine what are acceptable or not acceptable findings, based on the stringent criteria outlined above, and of pulling together research outcomes into meta-analytical inferences are an essential component of translational science, and of translational evidence-based dentistry (21). Moreover, Glick further correctly opines that *‘...unquestionably, daily clinical decision making...is still based on personal empirical data...’* (20).

Of course, this situation brings forth a fundamental lack of information about the evidence-based movement in dentistry that still persists among a large proportion of dental care providers. Concerted efforts must be sustained to continue to fill this knowledge gap among dentists through continuing education courses, among professional students through well-coordinated curricula (22) that emphasize and reinforce the evidence-based perspective, and through introductory courses for pre-dental students.

Evidence-Based versus Based on the Evidence: A Critical Distinction

The distinction was noted between dentistry based on the evidence, and evidence-based dentistry (6,10). In brief, this dichotomy can be stated as follows: On the one hand, the emerging and increasingly well-established evidence-based paradigm demands that all of the available research evidence be accessed, reviewed and appraised, so that a consensus statement of the best available evidence be generated and incorporated into revised clinical practice guidelines. By contrast, the traditional approach to dentistry that is based on the evidence of at best a handful of research papers suffers from an inherent bias of selection, and can be dangerously detrimental to patients.

Dentistry based on the evidence is driven by such principal motives as the dentist being inexperienced in the evidence-based process and paradigm—hence, we return to the need for continuing education. The dentist could also be using the restricted available time to do a quick survey of the research literature to pick and choose, as it were, this or that piece of evidence that appears at first glance to be most pertinent to the patient’s needs and wants.

Toward POEMs

The approach to select the evidence that seems appropriate to the clinical needs is what Glick refers to as the *‘...patient-oriented evidence that matters...clinician care very much about POEMs* (23), *about enhancing the patients’ quality of life, about improving function and esthetics and about cost outcomes...’* (20).

Be that as it may, clinicians must be concerned, first and foremost, in providing the treatment that is the most appropriate and the most beneficial for the patient. Stated otherwise, *‘...problems (with POEMs) arise when practitioners rely on these opinions before they have been challenged by scientific rigor...’* (20). The appropriate scientific rigor in this domain of science is the evidence-based process of systematic review (20) in dentistry, that is READ, as we defined it above as the process of research evaluation and appraisal in dentistry.

In conclusion, in the emerging specialty of evidence-based research in dentistry, as well as in medicine for transitioning into the health sciences of the XXI Century, POEMs are fine, so long as we READ!

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